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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte TAKASHI HORIGUCHI, HIDEKI MATSUI, and
TOMOMICHI WATANABE

Appeal 2010-003270
Application 10/547,843
Technology Center 1600

Before ERIC GRIMES, FRANCISCO C. PRATS, and
JEFFREY N. FREDMAN, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This is an appeal under 35 U.S.C. § 134 involving claims relating to a human protein. The Examiner has rejected the claims for indefiniteness and

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

lack of patentable utility. We have jurisdiction under 35 U.S.C. § 6(b). We reverse the indefiniteness rejection but affirm the rejection based on lack of utility.

STATEMENT OF THE CASE

The Specification discloses a protein, designated C1, encoded by a "gene whose expression was significantly increased upon application of endoplasmic reticulum stress to nerve cells" (Spec. 2: 13-14). The amino acid sequence of C1 is shown in the Specification's SEQ ID NO: 1 (*id.* at 68: 30-33).

Claims 1, 2, 4-7, and 17 are on appeal. Claims 1 and 17 are representative and read as follows:

> 1. An isolated protein, comprising the amino acid sequence of SEQ ID NO: 1, or a salt thereof.
>
> 17. A kit for screening a compound or its salt that promotes or inhibits the activity of the protein or its salt according to claim 1, which comprises the protein or its salt according to claim 1.

The claims stand rejected as follows:

- Claim 17 under 35 U.S.C. § 112, second paragraph, as indefinite (Answer 7); and
- Claims 1, 2, 4-7, and 17 under 35 U.S.C. §§ 101 and 112, first paragraph, on the basis that the Specification does not disclose a patentable utility for the claimed products (Answer 3, 7).

I.

The Examiner has rejected claim 17 as indefinite, on the ground that "[s]ince the activity of the protein of SEQ ID NO: 1 is not known . . . , and

because there appears to be no patentably significant utility in screening for compounds that affect the activity of the protein of SEQ ID NO: 1, one skilled in the art would now [sic, not] know as what material limitations define the claimed subject matter" (Answer 8).

Appellants contend that the rejection is in error because it "is premised on the allegation that the C1 protein is not sufficiently characterized" (Appeal Br. 19-20).

We will reverse this rejection. "A claim is indefinite if, when read in light of the specification, it does not reasonably apprise those skilled in the art of the scope of the invention." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1342 (Fed. Cir. 2003). Here, the claim is directed to a kit for screening compounds to identify those that inhibit or promote the activity of C1. The only structural requirement of the kit is that it comprise the protein of SEQ ID NO: 1 or a salt thereof; the intended use of the kit does not limit it structurally. The claim language, while broad, is not indefinite. *See In re Miller*, 441 F.2d 689, 693 (CCPA 1971) ("[B]readth is not to be equated with indefiniteness.").

II.

Issue

The Examiner has rejected claims 1, 2, 4-7, and 17 under 35 U.S.C. §§ 101 and 112, first paragraph, "because the claimed invention is not supported by either a specific and substantial credible asserted utility or a well-established utility" (Answer 3; *see also id.* at 7). The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii).

The Examiner finds that the Specification discloses that C1 and DNA encoding it can be used to prevent or treat neurodegenerative diseases but fails to explain how any of the properties disclosed for C1 relate to its use in treating neurodegenerative diseases, or Alzheimer's disease specifically (Answer 5). The Examiner also finds that "the experiments on cells with artificially altered genotype (overexpression of C1 gene) do not represent an art-accepted model to study neurodegeneration or specifically Alzheimer's disease" (*id.*). The Examiner concludes that "the instant specification does not disclose a credible 'real world' use for the encoded protein in . . . currently available form" and therefore does not satisfy the requirements of 35 U.S.C. § 101 (*id.* at 6-7).

Appellants contend that the claimed protein has utility because the Specification discloses a "nexus between C1 protein (i.e., SEQ ID NO: 1) and enhanced expression in nerve cells subjected to endoplasmic reticulum (ER) stress" (Appeal Br. 13). Appellants also contend that C1 has utility because the Specification discloses that it decreases secretion of Aβ peptide in human neuroblastoma cells transformed with DNA encoding C1 (*id.* at 14) and "Siemers et al. and Fleisher et al. report the use of the compound LY450139 (an inhibitor of γ-secretase, the enzyme that is involved in producing Aβ peptide from APP), having Aβ secretion inhibitory activity, as a therapeutic agent for Alzheimer's disease in clinical trials" (*id.* at 15, footnote omitted).

The issue with respect to this rejection is: Does the evidence of record support the Examiner's finding that the Specification does not

disclose a utility for the claimed protein that satisfies the requirements of 35 U.S.C. § 101?

Findings of Fact

1. The Specification discloses that in response to conditions such as heat shock and glucose starvation, "abnormal proteins are accumulated in endoplasmic reticula, thus stressing the endoplasmic reticula (endoplasmic reticulum stress)" (Spec. 1: 19-22).

2. The Specification discloses that "[w]hen the living body is subjected to endoplasmic reticulum stress, endoplasmic reticulum response genes including a chaperon [sic] molecule are expressed to repair or decompose the abnormal proteins thereby maintaining homeostasis" (*id.* at 1: 22-24).

3. The Specification discloses that rat nerve cells were treated with tunicamycin, thapsigargin, or 2-deoxyglucose and gene expression was analyzed using an oligonucleotide microarray, and "[a]s a result of comparison of gene expression profiles . . . , the expression of GeneBank No. 170665 was promoted by endoplasmic reticulum stress stimulation" by each of the three agents (*id.* at 65: 7-24).

4. The Specification discloses that expression of GenBank No. 170665 was promoted by addition of β-amyloid to the cell culture medium of rat nerve cells (*id.* at 66: 11-18).

5. The Specification discloses that C1 (SEQ ID NO: 1) is a human ortholog of GenBank No. 170665 (*id.* at 67: 6; 68: 30-35).

6. The Specification discloses that when SK-N-AS cells were transformed with an expression vector encoding C1 and treated with

tunicamycin, "DNA cleavage was promoted in the cells transformed with the C1 gene, as compared with . . . control cells" (*id.* at 69: 3-18). The Specification concludes that "C1 had an [sic] cell-death promoting action" (*id.* at 69: 19).

7. Appellants state that SK-N-AS cells are human neuroblastoma cells (Appeal Br. 14).

8. The Specification discloses that when IMR-32 cells were transformed with an expression vector encoding C1 and the culture supernatant was assayed for Aβ40 and Aβ42, concentrations of both Aβ peptides were reduced compared to control cells (Spec. 69: 22-33). The Specification concludes that "C1 had an inhibitory action on secretion of Aβ40 and Aβ42" (*id.* at 69: 34-35).

9. Appellants state that IMR-32 cells are human neuroblastoma cells (Appeal Br. 14).

10. The Examiner finds that "experiments on cells with artificially altered genotype (overexpression of C1 gene) do not represent an art-accepted model to study neurodegeneration or specifically Alzheimer's disease" (Answer 5).

11. The Specification discloses that C1 "can be used as a disease marker because its expression is increased upon application of endoplasmic reticulum stress to nerve cells" (Spec. 29: 29-30).

12. The Specification discloses that C1 is "useful as a diagnostic marker for neurodegenerative diseases" (*id.* at 70: 3-6).

13. The Specification discloses that "a pharmaceutical comprising an antisense polynucleotide [to the C1 gene], a compound or its salt inhibiting

the activity of [C1], or an antibody against [C1] can be used as a low-toxic prophylactic/therapeutic agent for neurodegenerative diseases" (*id.* at 29: 32 to 30: 1).

14. The Specification discloses that C1 and DNA encoding it "can be used as safe pharmaceuticals such as prophylactic/ therapeutic agents for diseases such as neurodegenerative diseases" (*id.* at 30: 21-23) because "where the DNA encoding [C1] is abnormal or deficient, or where the expression level of [C1] is reduced, there occur a variety of diseases, for example, neurodegenerative diseases" (*id.* at 30: 13-15).

15. The Specification discloses that "a compound or its salt that regulates (promotes or inhibits) the activities (for example, an [sic] cell-death promoting activity, β-amyloid production-inhibiting activity etc.) of [C1] is useful as a prophylactic/therapeutic agent for diseases, for example neurodegenerative diseases" (*id.* at 32: 35 to 33: 4).

16. The Specification discloses that C1 "can also be used as a β-amyloid production inhibitor" (*id.* at 30: 28-29).

17. The Specification discloses that a "compound promoting the activity of [C1], a compound promoting the expression of the gene for [C1], etc. can be used for example as a β-amyloid production inhibitor etc." (*id.* at 70: 17-19).

18. The Specification discloses that a "compound inhibiting the activity of [C1], a compound inhibiting the expression of the gene for [C1], etc. can be used for example as an [sic] cell-death inhibitor etc." (*id.* at 70: 19-21).

19. Siemers[2] discloses that "[a]myloid β (Aβ) may play a central role in the pathogenesis of Alzheimer disease" (Siemers 126 (abstract)).

20. Siemers discloses that "Aβ is formed by the cleavage of the amyloid precursor protein (APP), first at the β site followed by cleavage at the γ site" (*id.* at 126, right col.).

21. Siemers discloses that some "lines of evidence suggest that reduction in the synthesis of Aβ might slow the rate of disease progression" (*id.*).

22. Siemers discloses that "LY450139 is a functional γ-secretase inhibitor that reduces the rate of formation of Aβ" *in vitro* and in a mouse model of Alzheimer's disease (*id.*).

Principles of Law

A claimed invention must have a utility that is substantial and specific to satisfy 35 U.S.C. § 101. *In re Fisher*, 421 F.3d 1365, 1371 (Fed. Cir. 2005).

A substantial utility "show[s] that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research. Simply put, to satisfy the 'substantial' utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public." *Id.*

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[2] Siemers et al., "Safety, Tolerability, and Changes in Amyloid β Concentrations After Administration of a γ-Secretase Inhibitor in Volunteers," 28 Clin. Neuropharmacol. 126-132 (May 2005).

To satisfy the requirement of a specific utility, "an asserted use must . . . show that that claimed invention can be used to provide a well-defined and particular benefit to the public." *Id.*

"It is well established that the enablement requirement of § 112 incorporates the utility requirement of § 101." *Id.* at 1378.

"Enablement, or utility, is determined as of the application filing date." *In re Brana*, 51 F.3d 1560, 1567 n.19 (Fed. Cir. 1995).

Analysis

The Specification discloses that certain conditions cause abnormal proteins to accumulate in the endoplasmic reticulum (ER), leading to ER stress (FF 1), and that certain genes are expressed in response to ER stress "to repair or decompose the abnormal proteins thereby maintaining homeostasis" (FF 2). The Specification discloses that the C1 gene was identified as a gene whose expression was promoted by agents that cause ER stress (FFs 3-5).

The Specification discloses that C1 can be used as a disease marker based on its increased expression in cells subjected to ER stress (FF 11). The Specification, however, does not identify any diseases in which C1 is overexpressed, and for which C1 would consequently be a useful diagnostic marker. The Specification asserts that C1 is useful as a diagnostic marker for "neurodegenerative diseases" (FF 12), but does not provide or cite any evidence that the presence or absence of C1 is diagnostic for any particular disease. The asserted diagnostic utilities are therefore not substantial, because they are not a presently available benefit, or specific, because they do not provide a well-defined and particular benefit.

The Specification also asserts that C1 can be used to treat or prevent neurodegenerative diseases (FF 14). The Specification asserts the same utility for compounds that either promote or inhibit the activity of C1 (FFs 13, 15). Again, however, the Specification does not provide evidence or sound scientific reasoning to show that providing C1, promoting its activity, or inhibiting its activity has any effect in preventing or treating any specific neurodegenerative disease. The fact that the Specification asserts the same utility for compounds having diametrically opposed activities – promoting versus inhibiting the activity of C1 – supports a conclusion that the asserted utility was not in "presently available form" at the time the application was filed. The asserted utilities of C1 or compounds that regulate its activity as "prophylactic/therapeutic agents" are therefore neither substantial nor specific.

The Specification provides evidence that human neuroblastoma cells that are transformed with an expression vector encoding C1 are more susceptible to being killed by tunicamycin (FFs 6, 7) and secrete less Aβ40 and Aβ42 peptides (FFs 8, 9) than control cells. The Examiner, however, finds that the Specification's neuroblastoma cells are not an art-accepted model for neurodegenerative diseases in general, or Alzheimer's disease specifically (FF 10). Appellants have pointed to no evidence that contradicts the Examiner's finding or otherwise shows that the *in vitro* effects shown in the Specification indicate that C1 has a substantial and specific utility; i.e., that it provides a well-defined and presently available benefit to the public.

Appellants cite two references as disclosing "the use of the compound LY450139 (an inhibitor of γ-secretase, the enzyme that is involved in

producing Aβ peptide from APP), having Aβ secretion inhibitory activity, as a therapeutic agent for Alzheimer's disease in clinical trials" (Appeal Br. 15). The Fleisher reference cited by Appellants, however, was published in 2008, after the effective filing date of the present application. Appellants have not explained how the post-filing reference provides evidence of utility as of the filing date of the claimed invention and, therefore, we have not considered it.

The Siemers reference[3] was published before the effective filing date, but it does not state that "LY450139 . . . ha[s] Aβ secretion inhibitory activity," as Appellants assert. Siemers states that Aβ is formed from APP by cleavage at the β and γ sites (FF 20), that reduction in the synthesis (not secretion) of Aβ might slow the progression of Alzheimer's disease (FF 21), and that LY450139 is a γ-secretase inhibitor that reduces the rate of formation (not secretion) of Aβ (FF 22).

The evidence of record does not support Appellants' position that C1 would be expected to be useful because its activity is similar to that of LY450139. The Specification does not provide evidence that C1 is a γ-secretase inhibitor, and Siemers does not provide evidence that LY450139 inhibits secretion of Aβ peptide from neuroblastoma cells or that inhibiting secretion of Aβ from cells is a viable approach to treating Alzheimer's disease. Siemers therefore does not provide evidence showing that the Specification discloses a patentable utility for C1.

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[3] The Appeal Brief does not provide a citation for the Siemers reference but states that it was made of record on October 28, 2008. We understand the intended reference to be the one cited in footnote 2.

Conclusion of Law

The evidence of record supports the Examiner's finding that the Specification does not disclose a utility for the claimed C1 protein that satisfies the requirements of 35 U.S.C. § 101.

SUMMARY

We reverse the rejection of claim 17 under 35 U.S.C. § 112, second paragraph, and affirm the rejection of claims 1, 2, 4-7, and 17 under 35 U.S.C. §§ 101 and 112, first paragraph.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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